

Application No. 10/828,934  
Amdt. dated October 4, 2006  
Reply to Office Action of August 4, 2006

**Listing of Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

What is claimed is:

- 1 1. (Original) A partially thio-modified aptamer that binds to a TGF-beta protein.
- 1 2. (Original) The aptamer of claim 1, wherein the TGF-beta protein comprises a  
2 human TGF-beta.
- 1 3. (Original) The aptamer of claim 1, wherein the TGF-beta protein comprises a  
2 TGF-beta dimer.
- 1 4. (Original) The aptamer of claim 3, wherein the TGF-beta dimer is a homodimer.
- 1 5. (Original) The aptamer of claim 4, wherein the TGF-beta homodimer is a TGF-  
2 beta 1, 2 or 3 homodimer.
- 1 6. (Original) The aptamer of claim 3, wherein the TGF-beta dimer is a TGFbeta 1, 2  
2 or 3 heterodimer.
- 1 7. (Currently Amended) The aptamer of claim 1, wherein the aptamer comprises one  
2 or more thio-modifications as set forth in SEQ ID NOS: [[4-22]] 62.
- 1 8. (Original) The aptamer of claim 1, wherein the aptamer is achiral.
- 1 9. (Original) The aptamer of claim 1, wherein the aptamer further comprises a  
2 detectable label.
- 1 10. (Original) The aptamer of claim 1, further comprising one or more  
2 pharmaceutically acceptable salts.
- 1 11. (Original) The aptamer of claim 1, further comprising a diluent.

Application No. 10/828,934  
Amdt. dated October 4, 2006  
Reply to Office Action of August 4, 2006

1 12. (Withdrawn) A partially thio-modified aptamer that binds to a TGF-beta receptor.

1 13. (Withdrawn) The aptamer of claim 12, wherein the TGF-beta receptor is a  
2 signaling receptor.

1 14. (Withdrawn) The aptamer of claim 12, wherein the TGF-beta receptor is a co-  
2 receptor.

1 15. (Withdrawn) The aptamer of claim 13, wherein the TGF-beta signaling receptor  
2 comprises a human TGF-beta signaling receptor.

1 16. (Withdrawn) The aptamer of claim 13 wherein the TGF-beta signaling receptor  
2 comprises a TbetaRI or a TbetaRII receptor.

1 17. (Withdrawn) The aptamer of claim 13, wherein the target of the aptamer is the GS  
2 domain of a TbetaRI receptor.

1 18. (Withdrawn) The aptamer of claim 14, where the co-receptor is TGF-beta 3.

1 19. (Withdrawn) The aptamer of claim 12, wherein the aptamer is achiral.

1 20. (Withdrawn) A partially thio-modified aptamer that binds to a ligand-receptor  
2 complex comprising a TGF-beta ligand and a receptor complex comprising a TbetaRI and  
3 a TbetaRII receptors.

1 21. (Withdrawn) The aptamer of claim 20, wherein the target of the aptamer is the GS  
2 domain of a TbetaRI receptor.

1 22. (Withdrawn) The aptamer of claim 20, wherein the aptamer is achiral.

1 23. (Withdrawn) A partially thio-modified aptamer that binds to a ligand binding trap  
2 capable of trapping TGF-beta ligands.

1 24. (Withdrawn) The aptamer of claim 23, wherein the ligand binding trap comprises  
2 decorin, latency-associated protein (LAP) or alpha-macroglobulin.

Application No. 10/828,934  
Amdt. dated October 4, 2006  
Reply to Office Action of August 4, 2006

- 1 25. (Withdrawn) The aptamer of claim 23, wherein the aptamer is achiral.
- 1 26. (Withdrawn) A partially thio-modified aptamer that binds to an auxiliary protein  
2 that promotes binding of TGF-beta ligand to Tbeta signaling receptors.
- 1 27. (Withdrawn) The aptamer of claim 26, wherein the auxiliary protein is a SARA  
2 protein.
- 1 28. (Withdrawn) The aptamer of claim 26, wherein the aptamer is achiral.
- 1 29. (Withdrawn) A partially thio-modified aptamer that binds to a Smad protein.
- 1 30. (Withdrawn) The aptamer of claim 29, wherein the Smad protein is an R-Smad, a  
2 Co-Smad, an I-Smad or a combination thereof.
- 1 31. (Withdrawn) The aptamer of claim 29, wherein the aptamer is achiral.
- 1 32. (Withdrawn) A partially thio-modified aptamer that binds to a TGF-beta protein  
2 complex and enhances TGF-beta activity.
- 1 33. (Withdrawn) The aptamer of claim 32, wherein the binding site of the aptamer on  
2 the TGF-beta protein complex comprises a region of a ligand binding trap protein.
- 1 34. (Withdrawn) The aptamer of claim 32, wherein the binding site of the aptamer on  
2 the TGF-beta protein complex comprises a region of an inhibitory I-Smad.
- 1 35. (Withdrawn) The aptamer of claim 32, wherein the aptamer is achiral.
- 1 36. (Withdrawn) A partially thio-modified aptamer that binds to a TGF-beta protein  
2 complex and inhibits TGF-beta activity.
- 1 37. (Withdrawn) The aptamer of claim 36, wherein the binding site of the aptamer on  
2 the TGF-beta protein complex comprises a region of an R-Smad or a Co-Smad.
- 1 38. (Withdrawn) The aptamer of claim 36, wherein the aptamer is achiral.

Application No. 10/828,934  
Amtd. dated October 4, 2006  
Reply to Office Action of August 4, 2006

1 39. (Withdrawn) A partially modified thioaptamer that inhibits TGF-beta activity by  
2 binding to a TGF-beta ligand, a TGF-beta ligand-Tbeta receptor complex, a TGF-beta  
3 signaling receptor and co-receptor, to an R-Smad or a Co-Smad.

1 40. (Withdrawn) The aptamer of claim 39, wherein the aptamer is achiral.

1 41. (Withdrawn) A partially modified thioaptamer that modifies TGF-beta activity by  
2 binding to a TGF-beta ligand, a TGF-beta ligand-Tbeta receptor complex, a TGF-beta  
3 signaling receptor and co-receptor, to an R-Smad or a Co-Smad.

1 42. (Withdrawn) A method of inhibiting TGF- $\beta$  activity comprising the steps of:  
2 providing to a host in need of therapy a pharmaceutically effective amount of a  
3 thioaptamer that specifically binds to and inhibits TGF- $\beta$  activity.

1 43. (Withdrawn) The method of claim 42, wherein the thioaptamer is provided to the  
2 host to ameliorate the effects of: fibrosis, scarring and adhesion during wound healing;  
3 fibrotic diseases of the lung, liver and kidney; atherosclerosis, arteriosclerosis; cancers  
4 including gliomas, colon cancer, prostate cancer, breast cancer, neurofibromas, lung  
5 cancer; angiopathy, vasculopathy, nephropathy; systemic sclerosis; viral infections  
6 accompanied by immune suppression (HIV, HCV); and immunological disorders and  
7 deficiencies (auto-immune diseases).

1 44. (Withdrawn) A method of quantitating TGF- $\beta$  levels in a sample comprising the  
2 step of contacting a sample with a TGF- $\beta$ -specific thioaptamer.

1 45. (Withdrawn) The method of claim 44, wherein the samples comprises a  
2 physiological sample.

1 46. (Withdrawn) The method of claim 44, wherein the sample comprise a blood,  
2 tissue, cells, supernatant, media.

Application No. 10/828,934  
Amdt. dated October 4, 2006  
Reply to Office Action of August 4, 2006

1 47. (Withdrawn) The method of claim 44, wherein the TGF- $\beta$  protein comprises a  
2 human TGF- $\beta$ .

1 48. (Withdrawn) The method of claim 44, wherein the TGF- $\beta$  protein comprises a  
2 TGF- $\beta$  homodimer.

1 49. (Withdrawn) The method of claim 44, wherein the TGF- $\beta$  protein comprises a  
2 TGF- $\beta$ 1, 2 or 3 heterodimer.

1 50. (Withdrawn) The method of claim 44, wherein the thioaptamer comprises one or  
2 more thio-modifications as set forth in SEQ ID NOS.: 4-22.

1 51. (Withdrawn) The method of claim 44, wherein the thioaptamer further comprises  
2 a detectable label.

1 52. (Withdrawn) The method of claim 44, wherein the thioaptamer further comprises  
2 a detectable selected from the group consisting of a colorimetric, a fluorescent,  
3 a radioactive and an enzymatic agent.

1 53. (Withdrawn) A method of modulating TGF- $\beta$  signaling comprising the steps of:  
2 administering to a host a TGF- $\beta$  specific thioaptamer that modulates the activity through  
3 the TGF- $\beta$  receptor in a dosage effective to reduce activity of the TGF- $\beta$ .

1 54. (Withdrawn) The method of claim 53, wherein the thioaptamer modulates the  
2 activity through the TGF- $\beta$  receptor by increasing activity.

1 55. (Withdrawn) The method of claim 53, wherein the thioaptamer modulates the  
2 activity through the TGF- $\beta$  receptor by decreasing activity.

1 56. (Withdrawn) The method of claim 53, wherein the thioaptamer is selected from  
2 the group consisting of SEQ ID NOS.:4-22.

Application No. 10/828,934  
Amtd. dated October 4, 2006  
Reply to Office Action of August 4, 2006

- 1 57. (Withdrawn) A method of treating a pathological condition due to increased TGF-
- 2    β activity comprising the steps of:
- 3    administering to a host an effective dosage of a thioaptamer that modulates TGF-β.
- 1 58. (Withdrawn) The method of claim 57, wherein the thioaptamer binds to TGF-β, the TGF-β receptor, a TGF-β auxiliary protein, a TGF-β ligand binding trap protein or a TGF-β Smad protein.
- 1 59. (Withdrawn) The method of claim 57, wherein the thioaptamer modulates the activity through the TGF-β receptor by increasing activity.
- 1 60. (Withdrawn) The method of claim 57, wherein the thioaptamer modulates the activity through the TGF-β receptor by decreasing activity.
- 1 61. (Withdrawn) The method of claim 57, wherein the thioaptamer is selected from the group consisting of SEQ ID NOS.: 4-22.
- 1 62. (Withdrawn) The method of claim 57, wherein the pathological condition comprises:
  - 3 fibrosis, scarring and adhesion during wound healing; fibrotic diseases of the lung, liver and kidney; atherosclerosis and arteriosclerosis; cancers such as gliomas, colon cancer, prostate cancer, breast cancer, neurofibromas, lung cancer; angiopathy, vasculopathy, nephropathy; systemic sclerosis; viral infections accompanied by immune suppression (HIV, HCV); and immunological disorders and deficiencies (auto-immune diseases).
- 1 63. (Withdrawn) The method of claim 57, wherein the TGF-β specific thioaptamer is encapsulated.
- 1 64. (Withdrawn) The method of claim 57, wherein the capsule is degradable by an external stimulus to release the TGF-β specific thioaptamer.

Application No. 10/828,934  
Amdt. dated October 4, 2006  
Reply to Office Action of August 4, 2006

- 1 65. (Withdrawn) The method of claim 57, wherein the external stimulus is selected
- 2 from the group consisting of UV light, acid, water, in vivo enzymes, ultrasound and heat.
- 1 66. (Withdrawn) The method of claim 57, wherein the TGF- $\beta$  specific thioaptamer is
- 2 bound to a binding molecule.
- 1 67. (Withdrawn) The method of claim 57, wherein the TGF- $\beta$  specific thioaptamer is
- 2 bound to a binding molecule and further comprising the step of detaching the binding
- 3 molecule from the TGF- $\beta$  specific thioaptamer.
- 1 68. (Withdrawn) A method of treating a pathological condition in which increased
- 2 TGF- $\beta$  activity has been implicated comprising the steps of:
- 3 administering to a host a TGF- $\beta$  specific thioaptamer in a pharmaceutically acceptable
- 4 carrier at a dosage effective to reduce TGF- $\beta$  activity.
- 1 69. (Withdrawn) The method of claim 68, wherein the pharmaceutically acceptable
- 2 carrier is selected from the group consisting of a cream, gel, aerosol and powder for
- 3 topical application.
- 1 70. (Withdrawn) The method of claim 68, wherein the pharmaceutically acceptable
- 2 carrier is selected from the group consisting of a sterile solution for injection, irrigation
- 3 and inhalation.
- 1 71. (Withdrawn) The method of claim 68, wherein the pharmaceutically acceptable
- 2 carrier comprises a sterile dressing for topically covering a wound.
- 1 72. (Withdrawn) The method of claim 68, wherein the pharmaceutically acceptable
- 2 carrier is selected from the group consisting of a biopolymer and a polymer for
- 3 implanting within a wound.
- 1 73. (Withdrawn) The method of claim 68, further comprising the step of
- 2 administering a growth factor other than TGF- $\beta$ .

Application No. 10/828,934  
Amtd. dated October 4, 2006  
Reply to Office Action of August 4, 2006

1 74. (Withdrawn) The method of claim 68, wherein the TGF- $\beta$  specific thioaptamer is  
2 encapsulated.

1 75. (Withdrawn) A method of modulating TGF- $\beta$  signaling comprising the steps of:  
2 administering to a host a TGF- $\beta$  ligand binding trap specific thioaptamer that modulates  
3 the activity through the TGF- $\beta$  receptor in a dosage effective to reduce activity of the  
4 TGF- $\beta$ .

1 76. (Withdrawn) A method of modulating TGF- $\beta$  signaling comprising the steps of:  
2 administering to a host a TGF- $\beta$  auxiliary protein specific thioaptamer that modulates the  
3 activity through the TGF- $\beta$  receptor in a dosage effective to reduce activity of the TGF- $\beta$ .

1 77. (Withdrawn) A method of modulating TGF- $\beta$  signaling comprising the steps of:  
2 administering to a host a TGF- $\beta$  Smad protein specific thioaptamer that modulates the  
3 activity through the TGF- $\beta$  receptor in a dosage effective to reduce activity of the TGF- $\beta$ .